

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
PAMELA J. SHERWOOD
BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD ROAD, SUITE 200
MENLO PARK, CA 94025

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference UCSF-127WO2	Date of Mailing (day/month/year) 09 DEC 2003
International application No. PCT/US03/05291	International filing date (day/month/year) 20 February 2003 (20.02.2003)
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

Where? Directly to the International Bureau of WIPO, 34, chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 bis.1 and 90 bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer

Alexander H. Spiegler

Telephone No. (703) 308-0196

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UCSF-127WO2	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US03/05291	International filing date (<i>day/month/year</i>) 20 February 2003 (20.02.2003)	(Earliest) Priority Date (<i>day/month/year</i>) 20 February 2002 (20.02.2002)
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the Report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures

INTERNATIONAL SEARCH REPORT

International application No..

PCT/US03/05291

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-26

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/05291

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12N 5/02; C07H 21/02, 21/04
US CL : 435/6, 320, 325; 536/23.1, 23.5, 23.7

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 320, 325; 536/23.1, 23.5, 23.7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FAHAM et al. Mismatch Repair Detection (MRD): High-Throughput Scanning for DNA variations. Human Molecular Genetics. 2001, Vol. 10, No. 16, pages 1657-1664, see whole document.	1-25
---		-----
Y		26
X	WO 00/55369 A1 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 21 September 2000 (21.09.00), see whole document, especially pages 4-37.	1-24
---		-----
Y		25-26
Y	FAHAM et al. High Througput Scanning for Variations by Mismatch Repair Detection (MRD). American Journal of Human Genetics. October 1999, Vol. 65, No. 4, page A99, Abstract No. 517, see whole document.	1-26



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

14 November 2003 (14.11.2003)

Date of mailing of the international search report

09 DEC 2003

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703)305-3230

Authorized officer

Alexander H. Spiegler

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

PCT/US03/05291

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-26, drawn to methods of detecting a mismatch in a DNA duplex comprising detecting an alteration in a characteristic of a cell.

Group II, claim(s) 27-47, drawn to methods of detecting a mismatch in a DNA duplex by phenotypically sorting a plurality of distinct duplexes, identifying the duplexes in said phenotypically sorted population, wherein identification is effected by identifying at least one genotypically detectable genetic element.

Group III, claim(s) 48 and 50 (in part), drawn to improved vectors comprising a uniquely linked genotypically detectable element to the vector's standard sequence.

Group IV, claim(s) 49-52 (in part), drawn to improved vectors comprising an operably linked phenotypically sortable genetic element to a regulated strong promoter and a heterologous ribosomal binding site.

Group V, claim(s) 53, drawn to an improved mismatch repair vector comprising positioning the mismatch in the phenotypically sortable genetic element to be no more than 200 nucleotides from the test duplex.

Group VI, claim(s) 54, drawn to a method of preparing standard vectors for mismatch repair detection.

Group VII, claim(s) 55, drawn to a method of identifying alleles of a genomic locus.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The methods of Group I are directed to methods of detecting a mismatch in a DNA duplex comprising detecting an alteration in a characteristic of a cell, whereas the methods of Group II are directed to detecting a mismatch in a DNA duplex by phenotypically sorting a plurality of distinct duplexes, identifying the duplexes in said phenotypically sorted population, wherein identification is effected by identifying at least one genotypically detectable genetic element, whereas Groups III-V are drawn to vectors not used in Groups I or II, and are structurally and functionally distinct from each other, whereas the method of Group VI is directed to a method of preparing standard vectors for mismatch repair detection, whereas Group VII is directed to a method of identifying alleles of a genomic locus. Each of the methods (i.e., Groups I-II and VI-VII) lack the same or corresponding special technical features because they are drawn to different method steps, having different starting materials which accomplish different goals. Furthermore, the vectors of Groups III-V lack the same or corresponding special technical features from each other because they are structurally and functional unique, having no common structure. Accordingly, Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1.

INTERNATIONAL SEARCH REPORT

PCT/US03/05291

Continuation of B. FIELDS SEARCHED Item 3:

Databases: USPAT, PGPUB, EPO, JPO, Derwent, Medline, Biosis, CaPlus, Embase, Biotechds

Search Terms: mismatch, duplex, repair, corepair, marker, vector, bacterial methyl mismatch repair, E. coli dam directed mismatch repair

CHAPTER I
PCT TELEPHONE MEMORANDUM
FOR
LACK OF UNITY OF INVENTION



PCT No.: PCT/US03/05291

Examiner: Alexander H. Spiegler

Attorney spoken to: Pam Sherwood

Date of call: 13 November 2003

☐ Amount of payment approved:

☐ Deposit account number to be charged:

☐ Attorney elected to pay for ALL additional inventions

☐ Attorney elected to pay only for the additional inventions covered by

☐ Group(s):

-- encompassing --

☐ Claim(s):

☒ Attorney elected NOT to pay for any additional inventions, therefore, only the first claimed invention (Group I) covered by Claim(s) 1-26 has been searched.

☒ Attorney was orally advised that there is no right to protest for any group not paid for.

☒ Attorney was orally advised that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/ISA/210).

Time Limit For Filing A Protest

Applicant is hereby given 15 days from the mailing date of this Search Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 40.2, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

Detailed Reasons For Holding Lack of Unity of Invention:

Please See Continuation Sheet

Note: A copy of this form must be attached to the Search Report.

**ATTACHMENT TO CHAPTER I PCT TELEPHONE MEMORANDUM
FOR
LACK OF UNITY OF INVENTION**

Continuation of Detailed Reasons For Holding Lack of Unity of Invention:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-26, drawn to methods of detecting a mismatch in a DNA duplex comprising detecting an alteration in a characteristic of a cell.

Group II, claim(s) 27-47, drawn to methods of detecting a mismatch in a DNA duplex by phenotypically sorting a plurality of distinct duplexes, identifying the duplexes in said phenotypically sorted population, wherein identification is effected by identifying at least one genotypically detectable genetic element.

Group III, claim(s) 48 and 50 (in part), drawn to improved vectors comprising a uniquely linked genotypically detectable element to the vector's standard sequence.

Group IV, claim(s) 49-52 (in part), drawn to improved vectors comprising an operably linked phenotypically sortable genetic element to a regulated strong promoter and a heterologous ribosomal binding site.

Group V, claim(s) 53, drawn to an improved mismatch repair vector comprising positioning the mismatch in the phenotypically sortable genetic element to be no more than 200 nucleotides from the test duplex.

Group VI, claim(s) 54, drawn to a method of preparing standard vectors for mismatch repair detection.

Group VII, claim(s) 55, drawn to a method of identifying alleles of a genomic locus.

The inventions listed as Groups 1-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The methods of Group I are directed to methods of detecting a mismatch in a DNA duplex comprising detecting an alteration in a characteristic of a cell, whereas the methods of Group II are directed to detecting a mismatch in a DNA duplex by phenotypically sorting a plurality of distinct duplexes, identifying the duplexes in said phenotypically sorted population, wherein identification is effected by identifying at least one genotypically detectable genetic element, whereas Groups III-V are drawn to vectors not used in Groups I or II, and are structurally and functionally distinct from each other, whereas the method of Group VI is directed to a method of preparing standard vectors for mismatch repair detection, whereas Group VII is directed to a method of identifying alleles of a genomic locus. Each of the methods (i.e., Groups I-II and VI-VII) lack the same or corresponding special technical features because they are drawn to different method steps, having different starting materials which accomplish different goals. Furthermore, the vectors of Groups III-V lack the same or corresponding special technical features from each other because they are structurally and functional unique, having no common structure. Accordingly, Groups 1-VII do not relate to a single general inventive concept under PCT Rule 13.1.

Note: A copy of this form must be attached to the Search Report.